

In the Claims

Applicant has submitted a new complete claim set showing marked up claims with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing.

1. (Original) A composition comprising isolated PSMA protein, wherein at least 5% of the isolated PSMA protein is an isolated PSMA protein multimer.
2. (Original) The composition of claim 1, wherein the isolated PSMA protein multimer is an isolated PSMA protein dimer.
3. (Original) The composition of claim 2, wherein the isolated PSMA protein dimer comprises a fragment of full-length PSMA (SEQ ID NO: 1).
4. (Original) The composition of claim 2, wherein the isolated PSMA protein dimer comprises a fragment of the extracellular portion of PSMA (amino acids 44-750 of SEQ ID NO: 1).
5. (Original) The composition of claim 3, wherein the fragment comprises amino acids 58-750 of SEQ ID NO: 1.
6. (Original) The composition of claim 3, wherein the fragment comprises amino acids 44-750 of SEQ ID NO: 1.
7. (Original) The composition of claim 3, wherein the fragment comprises amino acids 601-750 of SEQ ID NO: 1.
8. (Original) The composition of claim 2, wherein at least 25% of the isolated PSMA protein is in the form of an isolated PSMA protein dimer.

9. (Original) The composition of claim 2, wherein at least 50% of the isolated PSMA protein is in the form of an isolated PSMA protein dimer.
10. (Original) The composition of claim 2, wherein at least 75% of the isolated PSMA protein is in the form of an isolated PSMA protein dimer.
11. (Original) The composition of claim 2, wherein at least 90% of the isolated PSMA protein is in the form of an isolated PSMA protein dimer.
12. (Original) The composition of claim 2, wherein at least 95% of the isolated PSMA protein is in the form of an isolated PSMA protein dimer.
13. (Previously Presented) The composition of claim 1, wherein the composition further comprises at least 0.25 molar equivalents of metal ion to PSMA protein.
14. (Original) The composition of claim 13, wherein the composition comprises at least 0.5 molar equivalents of metal ion to PSMA protein.
15. (Original) The composition of claim 13, wherein the composition comprises at least 1 molar equivalent of metal ion to PSMA protein.
16. (Original) The composition of claim 13, wherein the composition comprises a molar excess of metal ion to PSMA protein.
17. (Previously Presented) The composition of claim 1, wherein the composition is in a liquid or lyophilized form.
18. (Previously Presented) The composition of claim 1, wherein the composition further comprises an adjuvant.

19. (Currently Amended) The composition of claim 18, wherein the adjuvant is alum, monophosphoryl lipid A, ~~a-sapenin~~, an immunostimulatory oligonucleotide, incomplete Freund's adjuvant, complete Freund's adjuvant, montanide, vitamin E, a water-in-oil emulsions prepared from a biodegradable oil, Quil A, a MPL and mycobacterial cell wall skeleton combination, ENHANZYN™, CRL-1005, L-121, alpha-galactosylceramide or a combination thereof.
20. (Original) The composition of claim 19, wherein the adjuvant is alum.
21. (Previously Presented) The composition of claim 1, wherein the composition further comprises a cytokine.
22. (Previously Presented) The composition of claim 1, wherein the composition is sterile.
23. (Previously Presented) The composition of claim 1, wherein the composition is free of chelating agents.
24. (Previously Presented) The composition of claim 1, wherein the composition further comprises at least one buffer.
25. (Original) The composition of claim 24, wherein the at least one buffer is PBS (phosphate buffered saline), citric acid, sodium citrate, sodium acetate, acetic acid, sodium phosphate, phosphoric acid, sodium ascorbate, tartartic acid, maleic acid, glycine, sodium lactate, lactic acid, ascorbic acid, imidazole, sodium bicarbonate, carbonic acid, sodium succinate, succinic acid, histidine, sodium benzoate, benzoic acid or a combination thereof.
26. (Previously Presented) The composition of claim 1, wherein the composition further comprises a free amino acid, wherein the free amino acid is naturally occurring or non-naturally occurring.

27. (Original) The composition of claim 26, wherein the naturally occurring or non-naturally occurring free amino acid is a non-acidic free amino acid.
28. (Original) The composition of claim 27, wherein the non-acidic free amino acid is glycine, proline, isoleucine, leucine, alanine, arginine or a combination thereof.
29. (Previously Presented) The composition of claim 1, wherein the composition further comprises a surfactant.
30. (Original) The composition of claim 29, wherein the surfactant is Tween20, Tween80, Triton X-100, dodecylmaltoside, cholic acid, CHAPS or a combination thereof.
31. (Previously Presented) The composition of claim 1, wherein the composition further comprises a cryoprotectant, an antioxidant, a preservative or a combination thereof.
32. (Original) The composition of claim 31, wherein the cryoprotectant is a sugar, a polyol, an amino acid, a polymer, an inorganic salt, an organic salt, trimethylamine N-oxide, sarcosine, betaine, gamma-aminobutyric acid, octapine, alanopine, strombine, dimethylsulfoxide or ethanol.
33. (Original) The composition of claim 32, wherein the sugar is sucrose, lactose, glucose, trehalose or maltose.
34. (Original) The composition of claim 32, wherein the polyol is inositol, ethylene glycol, glycerol, sorbitol, xylitol, mannitol or 2-methyl-2,4-pentane-diol.
35. (Original) The composition of claim 32, wherein the amino acid is Na glutamate, proline, alpha-alanine, beta-alanine, glycine, lysine-HCl or 4-hydroxyproline.
36. (Original) The composition of claim 32, wherein the polymer is polyethylene glycol, dextran or polyvinylpyrrolidone.

37. (Original) The composition of claim 32, wherein the inorganic salt is sodium sulfate, ammonium sulfate, potassium phosphate, magnesium sulfate or sodium fluoride.

38. (Original) The composition of claim 32, wherein the organic salt is sodium acetate, sodium polyethylene, sodium caprylate, proprionate, lactate or succinate.

39. (Original) The composition of claim 31, where the antioxidant is ascorbic acid, an ascorbic acid derivative, butylated hydroxy anisole, butylated hydroxy toluene, alkylgallate, dithiothreitol (DTT), sodium meta-bisulfite, sodium bisulfite, sodium dithionite, sodium thioglycollic acid, sodium formaldehyde sulfoxylate, tocopherol, a tocopherol derivative, monothioglycerol or sodium sulfite.

40. (Original) The composition of claim 39, wherein the ascorbic acid derivative is ascorbylpalmitate, ascorbylstearate, sodium ascorbate or calcium ascorbate.

41. (Original) The composition of claim 39, wherein the tocopherol derivative is d-alpha tocopherol, d-alpha tocopherol acetate, dl-alpha tocopherol acetate, d-alpha tocopherol succinate, beta tocopherol, delta tocopherol, gamma tocopherol or d-alpha tocopherol polyoxyethylene glycol 1000 succinate.

42. (Original) The composition of claim 31, wherein the preservative is benzalkonium chloride, chlorobutanol, parabens, thimerosal, benzyl alcohol or phenol.

43. (Original) A composition comprising isolated multimeric PSMA protein, wherein the composition comprises less than 35% of a monomeric PSMA protein.

44. (Original) The composition of claim 43, wherein the isolated multimeric PSMA protein is an isolated dimeric PSMA protein.

45. (Previously Presented) The composition of claim 43, wherein the composition comprises less than 20% of the monomeric PSMA protein.
46. (Original) The composition of claim 45, wherein the composition comprises less than 15% of the monomeric PSMA protein.
47. (Original) The composition of claim 46, wherein the composition comprises less than 5% of the monomeric PSMA protein.
48. (Original) A composition comprising PSMA protein in a solution that promotes or preserves multimeric association of PSMA protein.
49. (Original) The composition of claim 48, wherein the solution that promotes or preserves multimeric association of PSMA protein is a solution that promotes or preserves dimeric association of PSMA protein.
50. (Previously Presented) The composition of claim 48, wherein the solution that promotes or preserves dimeric association of PSMA protein has a pH that ranges from 4 to 8.
51. (Original) The composition of claim 50, wherein the solution that promotes or preserves dimeric association of PSMA protein has a pH that ranges from 5 to 7.
52. (Original) The composition of claim 51, wherein the solution that promotes or preserves dimeric association of PSMA protein has a pH that ranges from 5.5 to 7.
53. (Original) The composition of claim 51, wherein the solution that promotes or preserves dimeric association of PSMA protein has a pH of 6.
54. (Previously Presented) The composition of claim 48, wherein the solution that promotes or preserves dimeric association of PSMA protein comprises a salt.

55. (Original) The composition of claim 54, wherein the cationic component of the salt is sodium, potassium, ammonium, magnesium, calcium, zinc or a combination thereof, and wherein the anionic component of the salt is chloride, sulfate, acetate or a combination thereof.

56. (Original) The composition of claim 55, wherein the salt is sodium chloride, sodium sulfate, sodium acetate or ammonium sulfate.

57. (Original) The composition of claim 56, wherein the salt is present at a concentration in the range of 50mM to 2M.

58. (Original) The composition of claim 57, wherein the salt is present at a concentration in the range of 100mM to 300mM.

59. (Original) The composition of claim 58, wherein the salt is present at a concentration of 150mM.

60. (Original) The composition of claim 57, wherein the composition further comprises an adjuvant.

61. (Original) The composition of claim 57, wherein the composition is physiologically acceptable.

62. (Previously Presented) The composition of claim 48, wherein the solution that promotes or preserves dimeric association of PSMA protein comprises metal ions.

63. (Original) The composition of claim 62, wherein the metal ions are zinc ions, calcium ions, magnesium ions, cobalt ions, manganese ions or a combination thereof.

64. (Original) The composition of claim 63, wherein the metal ions are zinc ions and calcium ions.

65. (Original) The composition of claim 64, wherein the zinc ions and calcium ions are present at a concentration in the range of 0.1mM to 5mM.

66. (Original) The composition of claim 64, wherein the zinc ions are present at a concentration that is lower than the concentration of the calcium ions.

67. (Original) The composition of claim 66, wherein the zinc ions are present at a concentration of 0.1mM and the calcium ions are present at a concentration of 1mM.

68. (Original) The composition of claim 63, wherein the metal ions are magnesium ions.

69. (Original) The composition of claim 68, wherein the magnesium ions are present at a concentration in the range of 0.1mM to 5mM.

70. (Original) The composition of claim 69, wherein the magnesium ions are present at a concentration of 0.5mM.

71. (Previously Presented) The composition of claim 48, wherein the solution that promotes or preserves dimeric association of PSMA protein is free of chelating agents.

72. (Previously Presented) The composition of claim 48, wherein the composition further comprises at least one buffer.

73. (Original) The composition of claim 72, wherein the at least one buffer is PBS (phosphate buffered saline), citric acid, sodium citrate, sodium acetate, acetic acid, sodium phosphate, phosphoric acid, sodium ascorbate, tartartaric acid, maleic acid, glycine, sodium lactate,

lactic acid, ascorbic acid, imidazole, sodium bicarbonate, carbonic acid, sodium succinate, succinic acid, histidine, sodium benzoate, benzoic acid or a combination thereof.

74. (Currently Amended) The composition of claim 48, wherein the composition further comprises a free amino acid, wherein the free amino acid is naturally occurring or non-naturally occurring.

75. (Original) The composition of claim 74, wherein the naturally occurring or non-naturally occurring free amino acid is a non-acidic free amino acid.

76. (Original) The composition of claim 75, wherein the non-acidic free amino acid is glycine, proline, isoleucine, leucine, alanine, arginine or a combination thereof.

77. (Previously Presented) The composition of claim 48, wherein the composition further comprises a surfactant.

78. (Original) The composition of claim 77, wherein the surfactant is Tween20, Tween80, Triton X-100, dodecylmaltoside, cholic acid, CHAPS or a combination thereof.

79. (Previously Presented) The composition of claim 48, wherein the composition further comprises a cryoprotectant, an antioxidant, a preservative or a combination thereof.

80. (Original) The composition of claim 79, wherein the cryoprotectant is a sugar, a polyol, an amino acid, a polymer, an inorganic salt, an organic salt, trimethylamine N-oxide, sarcosine, betaine, gamma-aminobutyric acid, octapine, alanopine, strombine, dimethylsulfoxide or ethanol.

81. (Original) The composition of claim 80, wherein the sugar is sucrose, lactose, glucose, trehalose or maltose.

82. (Original) The composition of claim 80, wherein the polyol is inositol, ethylene glycol, glycerol, sorbitol, xylitol, mannitol or 2-methyl-2,4-pentane-diol.
83. (Original) The composition of claim 80, wherein the amino acid is Na glutamate, proline, alpha-alanine, beta-alanine, glycine, lysine-HCl or 4-hydroxyproline.
84. (Original) The composition of claim 80, wherein the polymer is polyethylene glycol, dextran or polyvinylpyrrolidone.
85. (Original) The composition of claim 80, wherein the inorganic salt is sodium sulfate, ammonium sulfate, potassium phosphate, magnesium sulfate or sodium fluoride.
86. (Original) The composition of claim 80, wherein the organic salt is sodium acetate, sodium polyethylene, sodium caprylate, proprionate, lactate or succinate.
87. (Original) The composition of claim 79, where the antioxidant is ascorbic acid, an ascorbic acid derivative, butylated hydroxy anisole, butylated hydroxy toluene, alkylgallate, dithiothreitol (DTT), sodium meta-bisulfite, sodium bisulfite, sodium dithionite, sodium thioglycollic acid, sodium formaldehyde sulfoxylate, tocopherol, a tocopherol derivative, monothioglycerol or sodium sulfite.
88. (Original) The composition of claim 87, wherein the ascorbic acid derivative is ascorbylpalmitate, ascorbylstearate, sodium ascorbate or calcium ascorbate.
89. (Original) The composition of claim 87, wherein the tocopherol derivative is d-alpha tocopherol, d-alpha tocopherol acetate, dl-alpha tocopherol acetate, d-alpha tocopherol succinate, beta tocopherol, delta tocopherol, gamma tocopherol or d-alpha tocopherol polyoxyethylene glycol 1000 succinate.

90. (Original) The composition of claim 79, wherein the preservative is benzalkonium chloride, chlorobutanol, parabens, thimerosal, benzyl alcohol or phenol.

91. (Previously Presented) The composition of claim 48, wherein the composition is stable when stored at -80°C.

92. (Previously Presented) The composition of claim 48, wherein the composition is stable when stored at -20°C.

93. (Previously Presented) The composition of claim 48, wherein the composition is stable when stored at 4° C.

94. (Previously Presented) The composition of claim 39, wherein the composition is stable when stored at room temperature.

95. (Original) A composition comprising isolated PSMA protein in a solution that promotes or preserves dimeric association of PSMA protein wherein the solution comprises:

(a) 5 to 20mM of sodium phosphate, sodium acetate or a combination thereof,

(b) 100 to 300mM sodium chloride or sodium sulfate, and

(c) 0.1 to 2mM of at least one metal ion.

96. (Original) The composition of claim 95, wherein the solution has a pH in the range of 4 to 8.

97. (Original) The composition of claim 96, wherein the solution has a pH in a range of 5 to 7.

98. (Original) The composition of claim 97, wherein the solution has a pH in a range of 6 to 6.5.

99. (Original) The composition of claim 96, wherein the composition further comprises an adjuvant.

100. (Original) The composition of claim 99, wherein the adjuvant is alum.

101. (Original) The composition of claim 95, wherein the metal ion is a zinc ion, calcium ion, magnesium ion, cobalt ion, manganese ion or a combination thereof.

102-168. (Canceled)

169. (Withdrawn and Previously Presented) A method of treating a subject to elicit or enhance an immune response to cells in the subject expressing PSMA, comprising administering to the subject an effective amount of the composition of claim 1.

170. (Withdrawn and Currently Amended) The method of claim 169 [[171]], wherein the expressed PSMA is expressed on the cell surface.

171. (Withdrawn and Original) The method of claim 169, wherein the method further comprises administering one or more booster doses of a composition comprising PSMA protein.

172. (Withdrawn and Original) The method of claim 171, wherein the composition comprising PSMA protein is a composition of PSMA protein dimer.

173. (Withdrawn and Original) The method of claim 171, wherein the booster dose composition further comprises an adjuvant.

174. (Withdrawn and Previously Presented) The method of claim 171, wherein the booster dose composition is the composition of claim 1.

175. (Withdrawn and Original) The method of claim 169, wherein the composition is administered by intravenous, intramuscular, subcutaneous, parenteral, spinal, intradermal or epidermal administration.

176. (Withdrawn and Original) The method of claim 175, wherein the composition is administered by subcutaneous administration.

177. (Withdrawn and Original) The method of claim 169, wherein the subject has cancer or has been treated for cancer.

178. (Withdrawn and Original) The method of claim 177, wherein the cancer is a primary tumor or is metastatic cancer.

179. (Withdrawn and Original) The method of claim 177, wherein the subject has prostate cancer.

180. (Withdrawn and Previously Presented) A method of eliciting an immune response, comprising administering to a subject an effective amount of the composition of claim 1.

181. (Withdrawn and Original) The method of claim 180, wherein the method further comprises administering one or more booster doses of a composition comprising PSMA protein.

182. (Withdrawn and Original) The method of claim 181, wherein the composition comprising PSMA protein is a composition PSMA protein dimer.

183. (Withdrawn and Original) The method of claim 181, wherein the booster dose composition further comprises an adjuvant.

184. (Withdrawn and Previously Presented) The method of claim 181, wherein the booster dose composition is the composition of claim 1.

185. (Withdrawn and Original) The method of claim 180, wherein the composition is administered by intravenous, intramuscular, subcutaneous, parenteral, spinal, intradermal or epidermal administration.

186. (Withdrawn and Original) The method of claim 185, wherein the composition is administered by subcutaneous administration.

187. (Previously Presented) A kit which comprises the composition of claim 1 and instructions for use.

188. (Previously Presented) A kit which comprises the composition of claim 22, an adjuvant and instructions for mixing.

189. (Original) The kit of claim 188, wherein the adjuvant is alum.

190. (Previously Presented) A kit which comprises the composition of claim 22, a diluent and instructions for mixing.

191. (Previously Presented) The kit of claim 187, wherein the composition is provided in a vial or ampoule with a septum or a syringe.

192. (Previously Presented) The kit of claim 187, wherein the composition is in lyophilized form.

193. (Previously Presented) A pharmaceutical composition comprising the composition of claim 1, and a pharmaceutically acceptable carrier.